

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) Microparticulate oral pharmaceutical dosage galenical form for the delayed and controlled release of at least one active principle (AP) --excluding perindopril--this active principle having an absorption window in vivo that is essentially limited to the upper parts of the gastrointestinal tract, ~~said form being designed so as to guarantee its therapeutic efficacy by guaranteeing its absorption in vivo,~~

wherein the dosage form comprises "reservoir" microcapsules of active principle, each coated with at least one coating film,

wherein the coating film comprising at least one hydrophilic polymer A carrying groups that are ionized at neutral pH, and at least one hydrophobic compound B;

wherein the at least one hydrophobic compound B is selected from the group consisting of the products which tradenames (trademarks) are the following: Dynasan, Cutina, Dub, Castorwax, Croduret, Compritol, Sterotex, Lubritab, Apifil, Akofine, Softtisan, Super Hartolan, Protalan, Akosoft, Akosol, Cremao, Massupol, Novata, Suppocire, Wecobee, Witepsol, Lanolin, Incromega, Estaram, Suppoweiss, Gelucire, Precirol, Emulcire, Plurol diisostearique, Geleol, Hydrine and Monthyle; and

wherein: ~~in that~~ the release of the active principle is governed by two different triggering mechanisms,

wherein the first triggering mechanism releases the at least one AP one being based on a variation in pH and

wherein the second triggering mechanism releases the at least one AP the other allowing
~~the release of the AP~~ after a predetermined residence time in the stomach,

wherein the in that its dissolution behavior of the pharmaceutical dosage in vitro
(~~determined as indicated in the European Pharmacopeia, 3rd edition, under the title: "Dissolution test for solid oral forms": type II dissolutest performed under SINK conditions, maintained at 37.degree. C. and agitated at 100 rpm~~) is such that: at a constant pH of 1.4, the dissolution profile includes a latency phase with a duration less than or equal to 5 hours, and the change from pH 1.4 to pH 6.8, ~~during the latency phase~~, results in a release phase that starts without a latency period.

2. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 1, wherein the dissolution profile includes a latency phase with a duration of between 1 and 5 hours.

3. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 1, wherein it comprises "reservoir" microcapsules containing at least one active principle ~~excluding perindopril—these microcapsules being of the type that: consist of particles of active principle each coated with at least one film, this coating film consisting of a composite material which: comprises: at least one hydrophilic polymer A carrying groups that are ionized at neutral pH, and at least one hydrophobic compound B; and~~

wherein the and represents a mass fraction of the coating film (% by weight, based on the total mass of the microcapsules) of ≤ 40 ; [[and]]

wherein said microcapsules have a diameter below 2000 microns, the coating film of these microcapsules consists of a composite based on A and B in which:

wherein the weight ratio B/A is between 0.45 and 1.0, and

wherein the hydrophobic compound B is ~~selected from products that are~~ crystalline in the solid state and ~~[[have]]~~ has a melting point T_{FB} such that $T_{FB} \geq 40^{\circ} \text{C}$.

4. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 3, wherein the microcapsules have a diameter of between 200 and 800 microns, wherein the weight ratio B/A is between 0.5 and 1.0 and wherein the hydrophobic compound B is selected from products that are crystalline in the solid state and have a melting point T_{FB} such that $40^{\circ} \text{C} \leq T_{FB} \leq 90^{\circ} \text{C}$.

5. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 3, wherein the at least one hydrophilic polymer A is selected from the group consisting of: (meth)acrylic acid polymers, alkyl (meth)acrylate polymers, (meth)acrylic acid/alkyl (e.g. methyl) (meth)acrylate copolymers, and mixtures thereof; cellulose derivatives, preferably cellulose acetate, and/or phthalate, hydroxypropyl methyl cellulose phthalate, [[and]] hydroxypropyl methyl cellulose acetate, and/or succinate; and mixtures thereof.

6. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 3, wherein the at least one hydrophilic polymer A is selected from the group consisting of: (meth)acrylic acid/ methyl(meth)acrylate copolymers, and mixtures thereof; cellulose acetate, and/or phthalate, hydroxypropyl methyl cellulose phthalate, [[and]] hydroxypropyl methyl cellulose acetate, and/or succinate; and mixtures thereof.

7. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim

3, wherein the at least one compound B further comprises a compound ~~[[is]]~~ selected from the group consisting of: ~~following group of products:~~ vegetable waxes, ~~taken on their own or in mixtures with one another;~~ hydrogenated vegetable oils, ~~taken on their own or in a mixture with one another;~~ monoesters of glycerol with at least one fatty acid, ~~and/or~~ diesters of glycerol with at least one fatty acid, ~~and/or~~ triesters of glycerol with at least one fatty acid, preferably glycerol esters of behenic acid, ~~taken by themselves or in a mixture with one another;~~ and mixtures thereof.

8. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim

3, wherein the at least one compound B further comprises a second compound ~~[[is]]~~ selected from the group consisting of: vegetable waxes, ~~taken on their own or in mixtures with one another;~~ hydrogenated vegetable oils, ~~taken on their own or in a mixture with one another;~~ ~~mixtures of~~ at least one monoester of glycerol with at least one fatty acid, ~~and of~~ at least one diester of glycerol with at least one fatty acid, ~~and/or of~~ at least one triester of glycerol with at least one fatty acid; and mixtures thereof.

9. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim

7 ~~[[or 8]]~~ wherein said second compound ~~the compound B~~ is selected from the group consisting of: ~~comprising~~ hydrogenated cottonseed oil, hydrogenated soybean oil, hydrogenated palm oil, glyceryl behenate, hydrogenated castor oil, tristearin, tripalmitin, trimyristin, wax yellow, suppository bases, ~~[[or]]~~ hard fat, anhydrous milk fat, lanolin, glyceryl palmitostearate,

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glycerylstearate, lauryl macroglycerides, cetyl alcohol, polyglyceryl diisostearate, diethylene glycol monostearate, ethylene glycol monostearate, Omega 3 and any mixtures thereof.

10. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 7 [[or 8]] wherein said second compound ~~the compound B~~ is selected from the group consisting of: hydrogenated cottonseed oil, hydrogenated soybean oil, hydrogenated palm oil, glyceryl behenate, hydrogenated castor oil, tristearin, tripalmitin, trimyristin and any mixtures thereof.

11. (Cancel).

12. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 3 wherein the at least one compound B is selected from the group consisting of ~~comprising~~ the products which tradenames (trademarks) are the following[[s]]: Dynasan P60, Dynasan 114, Dynasan 116, Dynasan 118, Cutina HR, ~~Hydrobase 66-68~~, Dub HPH, Compritol 888, Sterotex NF, Sterotex K, Lubritab and mixtures thereof.

13. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 3 wherein the coating film of the microcapsules is free from talc.

14. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 1, wherein, at a constant pH of 1.4, the controlled release phase following the latency phase is such that the release time for 50% of the active principle ($t_{1/2}$) is defined as follows (in hours):
 $0.25 \leq t_{1/2} \leq 35$.

15. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 1, characterized in that the release phase following the change from pH 1.4 to pH 6.8, which takes place without a latency period, is such that the release time for 50% of the AP ($t_{1/2}$) is defined as follows (in hours): $0.25 \leq t_{1/2} \leq 20$.

16. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 3, wherein the microcapsules comprise a single composite coating film AB.

17. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 3, wherein the active principle is deposited on a neutral core with a diameter of between 200 and 800 microns.

18. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 3, wherein the neutral core contains sucrose and/or dextrose and/or lactose.

19. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 18, wherein the neutral core is a cellulose microsphere.

20. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim 1, wherein the at least one active principle is selected from the group consisting of: ~~used belongs to at least one of the following families of active substances:~~ antiulcer agents, antidiabetics, anticoagulants, antithrombics, hypolipidemics, antiarrhythmics, vasodilators, antiangina agents,

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antihypertensives, vasoprotectors, fertility promoters, labor inducers and inhibitors,

contraceptives, antibiotics, antifungals, antivirals, anticancer agents, anti-inflammatories,

analgesics, antiepileptics, antiparkinsonian agents, neuroleptics, hypnotics, anxiolytics,

psychostimulants, antimigraine agents, antidepressants, antitussives, antihistamines and

antiallergics.

21. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim

20, wherein the active principle is selected from the group consisting of following compounds:

amoxicillin, metformin, acetylsalicylic acid, pentoxifyllin, prazosin, acyclovir, nifedipine,

diltiazem, naproxen, ibuprofen, flurbiprofen, ketoprofen, fenoprofen, indomethacin, diclofenac,

fentiazac, estradiol valerate, metoprolol, sulpiride, captopril, cimetidine, zidovudine, nicardipine,

terfenadine, atenolol, salbutamol, carbamazepine, ranitidine, enalapril, simvastatin, fluoxetine,

alprazolam, famotidine, ganciclovir, famciclovir, spironolactone, 5-asa, quinidine, morphine,

pentazocine, paracetamol, omeprazole, metoclopramide and mixtures thereof.

22. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim

1, wherein said pharmaceutical dosage form is selected from the group consisting of: which is a

~~form selected in the group comprising:~~ a tablet, a powder and a gelatin capsule.

23. (Cancel).

24. (Presently amended) ~~Galenical form~~ The pharmaceutical dosage form according to claim

1 [[or 23,]] which is a tablet that disperses in the mouth.